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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,329	06/10/2002	Robert P. Kimberly	UAB-16802/22	3608

25006 7590 09/26/2005

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EXAMINER

GOLDBERG, JEANINE ANNE

ART UNIT PAPER NUMBER

1634

DATE MAILED: 09/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/049,329

Applicant(s)

KIMBERLY ET AL.

Examiner

Jeanine A. Goldberg

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 August 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 9-15 is/are pending in the application.
- 4a) Of the above claim(s) 9-11 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 12-15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. This action is in response to the papers filed August 3, 2005. Currently, claims 1, 9-15 are pending. Claims 9-11 have been withdrawn as drawn to non-elected subject matter.
2. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow. This action is made FINAL.
3. Any objections and rejections not reiterated below are hereby withdrawn.

Maintained Rejections

Election/Restrictions

4. Applicant's election without traverse of Group I, Claims 1-8 in the paper filed December 27, 2004 is acknowledged.

The requirement is still deemed proper and is therefore made FINAL.

Priority

5. This application is a 371 of PCT/US/00/21769, filed August 9, 2000 and claims benefit to provisional application 60/147,838, filed August 9, 1999 and 60/153,869, filed September 14, 1999.

An incorporation-by-reference statement added after the filing date of an application is not permitted because no new matter can be added to an application after its filing date. See 35 U.S.C. § 132(a). If an incorporation-by-reference statement is included in an amendment to the specification to add a benefit claim after the filing date of the application, the amendment would not be proper. When a benefit claim is

submitted after the filing of an application, the reference to the prior application cannot include an incorporation-by-reference statement of the prior application. See Dart Industries v. Banner, 636 F.2d 684, 207 USPQ 273 (C.A.D.C. 1980). Therefore, the Office will not grant a petition to accept a benefit claim that includes an incorporation-by-reference statement of a prior application, unless the incorporation-by-reference statement was submitted on filing of the application. (see <http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/benefitclaims.pdf>)

Claim Rejections - 35 USC § 112-Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 12-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a process for determining IL-10 promoter alleles specific to an individual human using -3575 and -2763.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2b 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed". Applicant is reminded that Vas-

Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2b 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...' required a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

With respect to Newly amended Claims 1, 12-15, neither the specification nor the claims describe position -3575, -2849, -2763. The specification nor the claims provide any reference point for the positions or provide any sequence from which these positions are found. The specification nor the claims have described the positions - 3575, -2849, -2763.

Accordingly, Applicants have not adequately disclosed the relevant identifying characteristics of a representative number of species within the claimed genus.

Response to Arguments

The response traverses the rejection. The response asserts the specification describes not only the novel SNPs at -3575, -2849 and -2763, but further includes description of SNPS known in the art. The response asserts that the art teaches

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several polymorphisms which would allow positioning of the instant polymorphisms.

The response asserts that the specification references Eskdale, Genbank Sequence listings U16720 and X78437 and the references cited by the examiner. This argument has been thoroughly reviewed but not deemed persuasive because the art does not teach a uniform numbering system for these polymorphisms. The prior art teaches a RsaI polymorphism from C to A which is described as both -592 (Roh, Cancer Letters, Vol. 184, pages 57-63, 2002; Rood et al. Ann Rheum, Vol. 58, pages 85-89, February 1999), -627 (Eskdale, Immunogenetics, Vol. 46, pages 120-128, 1997) and -597 (Mok et al. Arthritis and Rheumatism, Vol. 41, No. 6, pages 1090-1095, June 1998) in the art. Further, the MaeIII polymorphisms from C to T is described as both -824, -854 and -819, respectively. Based upon the differences in numbering systems it is unclear where the instant polymorphisms fall.

The specification states that sequencing data from the region between -1.3kb and -4kb also showed single base differences compared to published IL-10 promoter sequences (Genbank entries U16720 and X78437). Upon review of these sequences, it is clear that X78437 has had three versions of the sequence since July 13, 1994. Among these changes, in July 2001, between the filing date of the instant application and the priority dates, the sequences was amended to add 5,000 additional nucleotides. It is clear that the Genbank entries have been amended prior and during the pendency of the instant application.

Specifically, looking to the changes made to X78437, GI14625939 and GI1167482, the annotations appear to indicate different mRNA start locations.

GI14625939 indicates position 9297 as the start site where as and GI1167482 indicates 4023. A blast comparison of these two locations indicates a 2 base pair difference in start sites. Therefore, counting into the promoter region would differ.

Turning to the Eskdale reference which is the 5' flanking sequence of the IL10 gene and comparing the X78437, GI14625939 similar confusion occurs. In the annotations of the X78437, GI14625939 reference, the -2744 mutation is located at nucleotide 6553. This position is located in a poly A region of 9 A's. Position -2744 of Eskdale is located nearly 35 base pairs downstream of this poly(A) region. Thus, there appear to be at least 3 numbering systems in the art which vary and it is unclear what is meant by -3575 and -2763.

Thus for the reasons above and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 112- Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1, 12-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

C) Newly amended Claims 1, 12-15 are indefinite over the recitation "said single nucleotide polymorphism is in nucleotide -***" because "-3575", for example, does not

have any context. The claims does not indicate –3575 of what sequence. Numbering systems in the art vary and it is not clear what –3575 encompasses.

Response to Arguments

The response traverses the rejection. The response asserts that the context of IL-10 promoter sequences known in the art at the time of filing, along with SNPs such as –1082, -819, -592 known in the art at the time of filing. This argument has been considered but is not convincing because the This argument has been thoroughly reviewed but not deemed persuasive because the art does not teach a uniform numbering system for these polymorphisms. The prior art teaches a RsaI polymorphism from C to A which is described as both -592 (Roh, Cancer Letters, Vo. 184, pages 57-63, 2002; Rood et al. Ann Rheum, Vol. 58, pages 85-89, February 1999), -627 (Eskdale, Immunogenetics, Vol. 46, pages 120-128, 1997) and -597 (Mok et al. Arthritis and Rheumatism, Vol. 41, No. 6, pages 1090-1095, June 1998) in the art. Further, the MaeIII polymorphisms from C to T is described as both -824, -854 and -819, respectively. Based upon the differences in numbering systems it is unclear where the instant polymorphisms fall.

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It is clear that the Genbank entries have been amended prior and during the pendency of the instant application.

Specifically, looking to the changes made to X78437, GI14625939 and GI1167482, the annotations appear to indicate different mRNA start locations. GI14625939 indicates position 9297 as the start site where as and GI1167482 indicates 4023. A blast comparison of these two locations indicates a 2 base pair difference in start sites. Therefore, counting into the promoter region would differ.

Turning to the Eskdale reference which is the 5' flanking sequence of the IL10 gene and comparing the X78437, GI14625939 similar confusion occurs. In the annotations of the X78437, GI14625939 reference, the -2744 mutation is located at nucleotide 6553. This position is located in a poly A region of 9 A's. Position -2744 of Eskdale is located nearly 35 base pairs downstream of this poly(A) region. Thus, there appear to be at least 3 numbering systems in the art which vary and it is unclear what is meant by -3575 and -2763.

Thus for the reasons above and those already of record, the rejection is maintained.

A1) Newly amended Claim 1, 12-15 are directed to alleles with "low IL-10 production." This recitation is indefinite because low is a relative term which does not clearly indicate the degree of low production. Furthermore, it is unclear from the language of the claim whether the claim requires determining promoter alleles or whether the claim requires determining promoter alleles associated with IL-10 production. The preamble of the method is drawn to determining IL-10 promoter alleles,

however the wherein clause of the method is directed at determining promoter alleles associated with IL-10 production. The claim could be amended to recite "A process for determining IL-10 promoter alleles specific to an individual human associated with IL-10 production, said process comprising the step of: genotyping DNA in an IL-10 promoter region for a single nucleotide polymorphism which affects IL-10 production, the single nucleotide polymorphism at a position selected from the group consisting of -3575 and -2763, said DNA being obtained from said individual human, said genotyping of said DNA resulting in determination of IL-10 promoter alleles specific to said individual human, wherein either an A at position -3575 is associated with low IL-10 production as compared to G at -3575, or an A at position -2763 is associated with low IL-10 production as compared with C at -2763."

B1) Claims 12-14 are indefinite over the haplotype A[G/A]A and "the haplotype TCG" because it is unclear what the haplotype specifically encompasses. Claim 12 is a method which uses position -3575 and -2763. Given the haplotype with what appears to be three positions, this is unclear. Further, Claim 13 appears to add -2849, however Claims 14-15 are not entirely clear the positions of "the haplotype TCG". The claim could be amended to recite "the haplotype of an A at position -3575, a G or A at position -2849 and an A at position -2763" for example.

Claim Objections

8. Claim 13 is objected to because of the following informalities. Newly added Claim 13 depend on Claim 11 which is a non-elected claim. Further, Claim 11 is not a

process claim. Claim 13 may more appropriately depend from either Claim 1 or Claim 12. Appropriate correction is required.

Conclusion

9. **No claims allowable.**

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

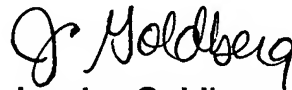
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272- 0745.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status

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information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Central Fax Number for official correspondence is (571) 273-8300.

A handwritten signature in black ink, appearing to read "J. Goldberg".

Jeanine Goldberg

Primary Examiner

September 15, 2005